Nutropin Depot®
[somatropin (rDNA origin) for injectable suspension]

DESCRIPTION

Nutropin Depot® [somatropin (rDNA origin) for injectable suspension] is a long-acting dosage form of recombinant human growth hormone (rhGH). Somatropin has 191 amino acid residues and a molecular weight of 22,125 daltons. The amino acid sequence of the product is identical to that of pituitary-derived human growth hormone. The protein is synthesized by a specific laboratory strain of *E. coli* as a precursor consisting of the rhGH molecule preceded by the secretion signal from an *E. coli* protein. This precursor is directed to the plasma membrane of the cell. The signal sequence is removed and the native protein is secreted into the periplasm so that the protein is folded appropriately as it is synthesized.

Somatropin is a highly purified preparation. Biological potency is determined using a cell proliferation bioassay.

The Nutropin Depot formulation consists of micronized particles of rhGH embedded in biocompatible, biodegradable polylactide-coglycolide (PLG) microspheres. Nutropin Depot is packaged in vials as a sterile, white to off-white, preservative-free, free-flowing powder. Before administration, the powder is suspended in Diluent for Nutropin Depot (a sterile aqueous solution).

Each 13.5 mg 3 cc single-use vial of Nutropin Depot contains 13.5 mg somatropin, 1.2 mg zinc acetate, 0.8 mg zinc carbonate, and 68.9 mg PLG.

Each 18 mg 3 cc single-use vial of Nutropin Depot contains 18 mg somatropin, 1.6 mg zinc acetate, 1.1 mg zinc carbonate, and 91.8 mg PLG.

Each 22.5 mg 3 cc single-use vial of Nutropin Depot contains 22.5 mg somatropin, 2.0 mg zinc acetate, 1.4 mg zinc carbonate, and 114.8 mg PLG.

Each dosage size contains an overage of rhGH microspheres to ensure delivery of labeled contents.

Each 1.5 mL single-use vial of Diluent for Nutropin Depot contains 30 mg/mL carboxymethylcellulose sodium salt, 1 mg/mL polysorbate 20, 9 mg/mL sodium chloride, and sterile water for injection; pH 5.8–7.2.

CLINICAL PHARMACOLOGY

General

In vivo preclinical and clinical testing has demonstrated that growth hormone (GH) stimulates longitudinal bone growth and elevates insulin-like growth factor-I (IGF-I) levels.

Actions that have been demonstrated for hGH include:

A. Tissue Growth - 1) Skeletal Growth: GH stimulates skeletal growth in pediatric patients with growth failure due to a lack of adequate secretion of endogenous GH. Skeletal growth is accomplished at the epiphyseal plates at the ends of a growing bone. Growth and metabolism of epiphyseal plate cells are directly stimulated by GH and one of its mediators, IGF-I. Serum levels of IGF-I are low in children and adolescents who are growth hormone deficient (GHD), but increase during treatment with GH. In pediatric patients, new bone is formed at the epiphyses in response to GH and IGF-I. This results in linear growth until these growth plates fuse at the end of puberty. 2) Cell Growth: Treatment with hGH results in an increase in both the number and the size of skeletal muscle cells. 3) Organ Growth: GH increases the size of internal organs, including kidneys, and increases red cell mass. Treatment of hypophysectomized or genetic dwarf rats with GH results in increases in organ and overall body growth. In normal rats subjected to nephrectomy-induced uremia, GH promoted skeletal and body growth.

B. Protein Metabolism - Linear growth is facilitated in part by GH-stimulated protein synthesis. This is reflected by nitrogen retention as demonstrated by a decline in urinary nitrogen excretion and blood urea nitrogen during GH therapy.

C. Carbohydrate Metabolism - GH is a modulator of carbohydrate metabolism. Patients with inadequate endogenous secretion of GH sometimes experience fasting hypoglycemia that is improved by treatment with GH. GH therapy may decrease insulin sensitivity. Administration of hGH formulated for daily dosing resulted in increased mean fasting and postprandial insulin levels, more commonly in overweight or obese individuals. Mean trough levels for fasting and postprandial insulin were unchanged after 3 or 6 months of Nutropin Depot therapy in GHD children. As with daily GH, mean trough levels for fasting glucose, postprandial glucose, and hemoglobin A_{1c} remained unchanged after 3 or 6 months of Nutropin Depot therapy.

D. Lipid Metabolism - In GHD patients, administration of GH formulated for daily dosing resulted in lipid mobilization, reduction in body fat stores, increased plasma fatty acids, and decreased plasma cholesterol levels.

E. Mineral Metabolism - The retention of total body potassium in response to GH administration apparently results from cellular growth. Serum levels of inorganic phosphorus may increase slightly in patients with inadequate secretion of endogenous GH due to metabolic activity associated with bone growth as well as increased tubular reabsorption of phosphate by the kidney. Serum calcium is not significantly altered in these patients. Sodium retention also occurs. (See PRECAUTIONS: Laboratory Tests.) GH therapy results in increases in serum alkaline phosphatase.

F. Connective Tissue Metabolism - GH stimulates the synthesis of chondroitin sulfate and collagen as well as the urinary excretion of hydroxyproline.

Pharmacokinetics

Nutropin Depot is a long-acting dosage form of somatropin designed to be administered by subcutaneous (SC) injection once or twice monthly. Following the injection, bioactive rhGH is released from the microspheres into the SC environment initially by diffusion, followed by both polymer degradation and diffusion. Although no studies have been performed that address the distribution, elimination, or metabolism of Nutropin Depot, once released and absorbed the rhGH is believed to be distributed and eliminated in a manner similar to somatropin formulated for daily administration.

The serum hGH concentration-time profiles of single doses of 0.75 mg/kg and 1.5 mg/kg of Nutropin Depot have been characterized in pediatric GHD patients (refer to Figure 1). The in vivo profiles are characterized by an initial rapid release followed by a slow decline in GH concentration. Both the maximum concentrations achieved (C_{max}) and total exposure ($AUC_{0-28\ days}$) appear to be proportional to dose. Serum hGH levels greater than 1 μg/L persist for approximately 11–14 days postdose for the two doses. Repeated dosing of Nutropin Depot over 6 months showed no progressive accumulation of GH.

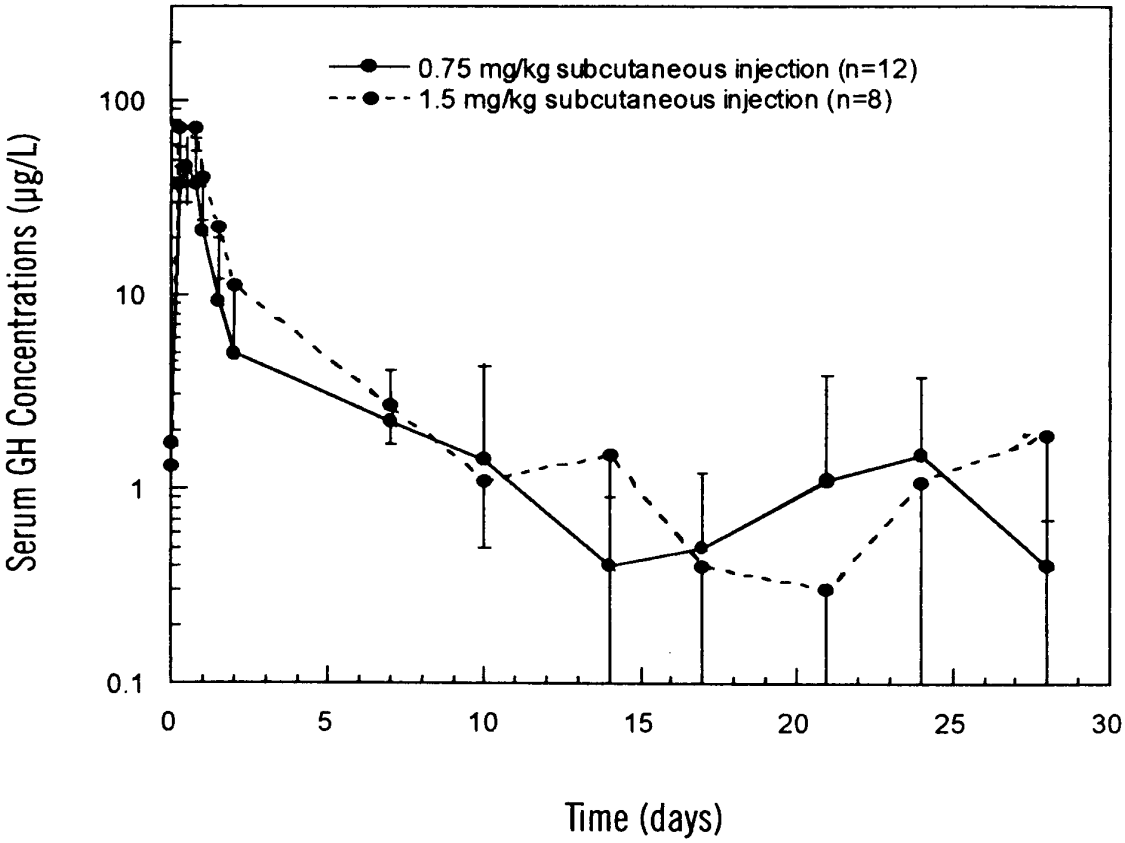
Absorption—In a study of Nutropin Depot in pediatric patients with GHD, an SC dose of 0.75 mg/kg (n = 12) or 1.5 mg/kg (n = 8) was administered. The mean ± SD hGH C_{max} values were 48±26 μg/L and 90±23 μg/L, respectively, at 12–13 hours postdose. The corresponding $AUC_{0-28\ days}$ values were 83±49 μg • day/L and 140±34 μg • day/L, respectively, for the two doses. For the 0.75 mg/kg and 1.5 mg/kg doses, the $AUC_{0-2days}$ accounted for approximately 52±16 percent and 61±10 percent of the total $AUC_{0-28\ days}$, respectively. Estimates of relative bioavailability in GHD children for a single dose of Nutropin Depot ranged from 33% to 38% when compared to a single dose of Nutropin AQ® [somatropin (rDNA origin) injection] in healthy adults, and from 48% to 55% when compared to chronically dosed Protropin® (somatrem for injection) in GHD children.

Distribution—Animal studies with rhGH formulated for daily administration showed that GH localizes to highly perfused organs, particularly the liver and kidney. The volume of distribution at steady state for rhGH formulated for daily administration in healthy adult males is about 50 mL/kg body weight, approximating the serum volume.

Metabolism—Both the liver and kidney have been shown to be important metabolizing organs for GH. Animal studies using rhGH formulated for daily administration suggest that the kidney is the dominant organ of clearance. GH is filtered at the glomerulus and reabsorbed in the proximal tubules. It is then cleaved within renal cells into its constituent amino acids, which return to the systemic circulation.

Elimination—The mean terminal $t_{1/2}$ after intravenous (IV) administration of rhGH formulated for daily administration in healthy adult males is estimated to be 19.5±3.1 minutes. Clearance of rhGH after IV administration in healthy adults and children is reported to be in the range of 116–174 mL/hr/kg.

Figure 1
Single-Dose Mean (SD) GH Concentrations in Pediatric GHD Patients



Special Populations

Pediatric—Available literature data suggest that rhGH clearances are similar in adults and children.

Gender—Following administration of either 0.75 mg/kg or 1.5 mg/kg Nutropin Depot, Day 1 GH levels were higher in females compared to males. No relationship was observed between gender and pharmacodynamic marker (IGF-I and IGFBP-3) levels.

Race—The effect of race on Nutropin Depot disposition is unknown due to the limited number of non-Caucasian patients in the Nutropin Depot studies.

Growth Hormone Deficiency—Nutropin Depot has not been studied in healthy adults or children. However, reported values for clearance of rhGH formulated for daily administration in adults and children with GHD range from 138–245 mL/hr/kg and are similar to those observed in healthy adults and children. Mean terminal $t_{1/2}$ values following IV and SC administration in adult and pediatric patients with GHD are also similar to those observed in healthy adult males.

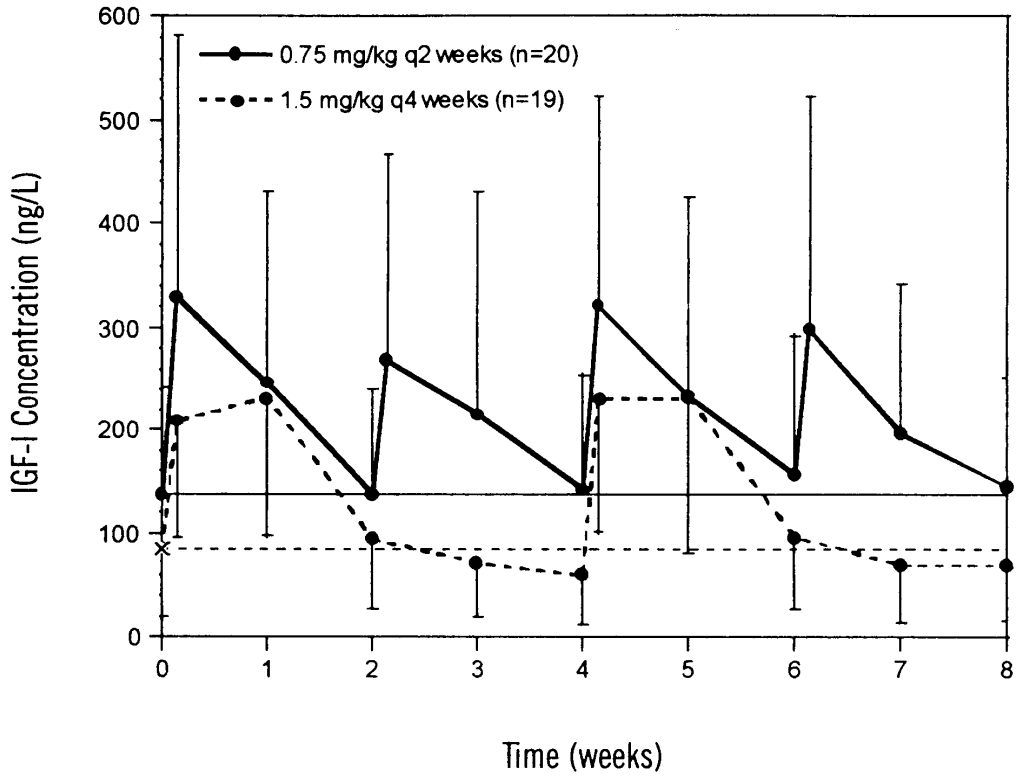
Renal Insufficiency—Nutropin Depot has not been studied in patients with renal insufficiency. Children and adults with chronic renal failure (CRF) and end-stage renal disease (ESRD) tend to have decreased clearance of rhGH formulated for daily administration compared with normals. Endogenous GH production may also increase in some individuals with ESRD. However, no GH accumulation has been reported in children with CRF or ESRD dosed with daily regimens.

Hepatic Insufficiency—Nutropin Depot has not been studied in patients with hepatic insufficiency. A reduction in clearance of rhGH formulated for daily administration has been noted in patients with severe liver dysfunction. The clinical significance of this decrease is unknown.

Pharmacodynamics

IGF-I levels peaked between 1.5 and 3.5 days postdose and remained above baseline for approximately 16 to 20 days, confirming GH activity for an extended period. Repeated dosing of Nutropin Depot over 6 months showed no progressive accumulation of IGF-I (as shown in Figure 2) or IGF-binding protein 3 (IGFBP-3).

Figure 2
Repeated-Dose Mean (SD) IGF-I Concentrations in Pediatric GHD Patients



Efficacy Studies

Pediatric Growth Hormone Deficiency (GHD)

In two multicenter, open-label clinical studies in prepubertal children (mean age (± SD) 7.4±2.8) with idiopathic or organic GHD previously untreated with rhGH, 91 patients were treated with Nutropin Depot at 1.5 mg/kg once monthly or 0.75 mg/kg twice monthly by subcutaneous injection for up to six months. (See DOSAGE AND ADMINISTRATION for the number of injections required per dose.) The mean prestudy growth rate was 4.8±2.4 cm/yr (n=89). The dose-pooled, mean 6-month annualized growth rate on Nutropin Depot therapy was 8.4±2.2 cm/yr (n=89).

Seventy-six patients continued treatment in an extension study. For patients who completed 12 months the mean growth rate was 7.8±1.9 cm/yr for the two dose groups combined (n=69). Mean height SD score changed from -3.0±1.0 prestudy to -2.5±0.9 at Month 12 (n=69). The mean 0 to 12 month change in bone age was 1.0±0.4 years (n=63). During the long-term extension study, fourteen of seventy-five (19%) patients discontinued due to dissatisfaction with growth response. Historical studies of GHD children treated with daily Protropin® (somatrem for injection) or Nutropin® [somatropin (rDNA origin) for injection] injections for 12 months at 0.3 mg/kg weekly had the

following mean values: baseline growth rate 3.6 to 4.8 cm/yr; first year growth rate 10.1 to 11.3 cm/yr; first year change in bone age 1.1 to 1.5 years.

In a dose-ranging study, 24 patients previously treated with daily GH (mean age 9.6±2.2 years; mean duration of prior GH therapy 2.8±1.6 yr, range 0.9 to 6.1 yr) were switched to Nutropin Depot therapy at the above doses. The mean growth rate on previous treatment was 8.2±3.0 cm/yr (range 3.2 to 13.1 cm/yr) and on Nutropin Depot was 5.1±2.0 cm/yr (range 2.4 to 9.6 cm/yr). During a long-term extension study, four of ten previously treated patients discontinued due to dissatisfaction with growth response. Historical studies of GHD children (n=181) treated with daily Protropin or Nutropin at a dose of 0.3 mg/kg weekly had the following mean growth rates: first year growth rate 9.7 to 11.4 cm/yr; second year growth rate 8.1 to 8.9 cm/yr; third year growth rate 7.5 to 7.8 cm/yr; fourth year growth rate 6.6 to 7.1 cm/yr.

INDICATIONS AND USAGE

Nutropin Depot® [somatropin (rDNA origin) for injectable suspension] is indicated for the long-term treatment of growth failure due to a lack of adequate endogenous GH secretion.

Considerations for use:—As with any GH treatment, patients should be monitored closely throughout therapy for growth response to Nutropin Depot. Failure to respond adequately requires careful assessment, as described under DOSAGE AND ADMINISTRATION. Patients for whom no discernible cause is found should be considered for a course of treatment with a daily form of rhGH. Experience in patients who were treated with daily GH and switched to Nutropin Depot is limited.

CONTRAINDICATIONS

Growth hormone should not be initiated to treat patients with acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma, or to patients having acute respiratory failure. Two placebo-controlled clinical trials in non-growth hormone–deficient adult patients (n = 522) with these conditions revealed a significant increase in mortality (41.9% vs. 19.3%) among somatropin-treated patients (doses 5.3–8 mg/day) compared to those receiving placebo (see WARNINGS).

Nutropin Depot should not be used for growth promotion in pediatric patients with closed epiphyses.

Nutropin Depot should not be used in patients with active neoplasia. GH therapy should be discontinued if evidence of neoplasia develops.

Growth hormone is contraindicated in patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment (see WARNINGS). Unless patients with Prader-Willi syndrome also have a diagnosis of growth hormone deficiency, Nutropin Depot is not indicated for the long term treatment of pediatric patients who have growth failure due to genetically confirmed Prader-Willi syndrome.

Revised language per FDA letter dated 30 March

WARNINGS

See CONTRAINDICATIONS for information on increased mortality in patients with acute critical illnesses in intensive care units due to complications following open heart or abdominal surgery, multiple accidental trauma, or with acute respiratory failure. The safety of continuing growth hormone treatment in patients receiving replacement doses for approved indications who concurrently develop these illnesses has not been established. Therefore, the potential benefit of treatment continuation with growth hormone in patients having acute critical illnesses should be weighed against the potential risk.

There have been reports of fatalities after initiating therapy with growth hormone in pediatric patients with Prader-Willi syndrome who had one or more of the following risk factors: severe obesity, history of upper airway obstruction or sleep apnea, or unidentified respiratory infection. Male patients with one or more of these factors may be at greater risk than females. Patients with Prader-Willi syndrome should be evaluated for signs of upper airway obstruction and sleep apnea before initiation of treatment with growth hormone. If, during treatment with growth hormone, patients show signs of upper airway obstruction (including onset of or increased snoring) and/or new onset sleep apnea, treatment should be interrupted. All patients with Prader-Willi syndrome treated with growth hormone should also have effective weight control and be monitored for signs of respiratory infection, which should be diagnosed as early as possible and treated aggressively (see CONTRAINDICATIONS). Unless patients with Prader-Willi syndrome also have a diagnosis of growth hormone deficiency, Nutropin Depot is not indicated for the long term treatment of pediatric patients who have growth failure due to genetically confirmed Prader-Willi syndrome.

Revised language per FDA letter dated 30 March

PRECAUTIONS

General: Nutropin Depot should be prescribed by physicians experienced in the diagnosis and management of patients with GHD.

Because GH may reduce insulin sensitivity, patients should be monitored for evidence of glucose intolerance.

For patients with diabetes mellitus, the insulin dose may require adjustment when GH therapy is instituted. Because GH may reduce insulin sensitivity, particularly in

obese individuals, patients should be observed for evidence of glucose intolerance. Patients with diabetes or glucose intolerance should be monitored closely during GH therapy.

Patients with symptomatic hypoglycemia associated with GHD should be closely monitored.

Patients with a history of an intracranial lesion should be examined frequently for progression or recurrence of the lesion. In pediatric patients, clinical literature has demonstrated no relationship between GH replacement therapy and central nervous system (CNS) tumor recurrence or new extracranial tumors.

Slipped capital femoral epiphysis may occur more frequently in patients with endocrine disorders or in patients undergoing rapid growth.

Progression of scoliosis can occur in patients who experience rapid growth. Because GH increases growth rate, patients with a history of scoliosis who are treated with GH should be monitored for progression of scoliosis. GH has not been shown to increase the incidence of scoliosis.

Intracranial hypertension (IH) with papilledema, visual changes, headache, nausea, and/or vomiting has been reported in a small number of patients treated with GH products. Symptoms usually occurred within the first 8 weeks of the initiation of GH therapy. In all reported cases, IH-associated signs and symptoms resolved after termination of therapy or a reduction of the GH dose. Funduscopic examination of patients is recommended at the initiation and periodically during the course of GH therapy.

As with any protein, local or systemic allergic reactions may occur. Parents/Patients should be informed that such reactions are possible and that prompt medical attention should be sought if allergic reactions occur (see ADVERSE REACTIONS).

Laboratory Tests: Serum levels of inorganic phosphorus, alkaline phosphatase, and parathyroid hormone (PTH) may increase with GH therapy.

Untreated hypothyroidism prevents optimal response to GH. Changes in thyroid hormone laboratory measurements may develop during GH treatment. Therefore, patients should have periodic thyroid function tests and should be treated with thyroid hormone when indicated.

Drug Interactions: Excessive glucocorticoid therapy will inhibit the growth-promoting effect of human GH. Patients with ACTH deficiency should have their glucocorticoid-replacement dose carefully adjusted to avoid an inhibitory effect on growth.

Limited published data indicate that GH treatment increases cytochrome P450 (CP450) mediated antipyrine clearance in humans. These data suggest that GH administration may alter the clearance of compounds known to be metabolized by CP450 liver enzymes (e.g., corticosteroids, sex steroids, anticonvulsants, cyclosporin). Careful monitoring is advisable when GH is administered in combination with other drugs known to be metabolized by CP450 liver enzymes.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenicity, mutagenicity, and fertility studies have not been conducted with Nutropin Depot.

Pregnancy Category C: Animal reproduction studies have not been conducted with Nutropin Depot. It is also not known whether Nutropin Depot can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nutropin Depot should be given to a pregnant woman only if clearly needed.

Nursing Mothers: It is not known whether GH is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Nutropin Depot is administered to a nursing mother.

Information for Patients: Patients being treated with Nutropin Depot and/or their parents should be informed of the potential benefits and risks associated with treatment. If home use is determined to be desirable by the physician, instructions on appropriate use should be given, including a review of the contents of the Patient Information Insert. This information is intended to aid in the safe and effective administration of the medication. It is not a disclosure of all possible adverse or intended effects.

If home use is prescribed, a puncture-resistant container for the disposal of used syringes and needles should be recommended to the patient. Patients and/or parents should be thoroughly instructed in the importance of proper disposal and cautioned against any reuse of needles and syringes (see Patient Information Insert).

ADVERSE REACTIONS

As with all protein pharmaceuticals, patients may develop antibodies to the protein. GH antibody-binding capacities below 2 mg/L have not been associated with growth attenuation. In some cases when binding capacity exceeds 2 mg/L, growth attenuation has been observed. In clinical studies of pediatric patients who were treated with Nutropin Depot, 0/138 patients with GHD screened for antibody production developed

antibodies with binding capacities ≥2 mg/L at any time during a treatment period of up to 17.4 months.

In addition to an evaluation of compliance with the prescribed treatment program and thyroid status, testing for antibodies to GH should be carried out in any patient who fails to respond to therapy.

In studies involving 138 pediatric patients treated with Nutropin Depot, the most frequent adverse reactions were injection-site reactions, which occurred in nearly all patients. On average, 2 to 3 injection-site adverse reactions were reported per injection. These reactions included nodules (61% of injections), erythema (53%), pain post-injection (47%), pain during injection (43%), bruising (20%), itching (13%), lipoatrophy (13%), and swelling or puffiness (8%). The intensity of these reactions was generally rated mild to moderate, with pain during injection occasionally rated as severe (7%).

Adverse reactions observed less frequently in the Nutropin Depot studies which were considered possibly, probably, or definitely related to the drug by the treating physician (usually occurring 1–3 days postdose) included: headache (13% of subjects), nausea (8%), lower extremity pain (7%), fever (7%), and vomiting (5%). These symptoms were generally self-limited and well-tolerated. One patient experienced a generalized body rash that was most likely an allergic reaction to Nutropin Depot.

Leukemia has been reported in a small number of GHD patients treated with GH. It is uncertain whether this increased risk is related to the pathology of GH deficiency itself, GH therapy, or other associated treatments such as radiation therapy for intracranial tumors. On the basis of current evidence, experts cannot conclude that GH therapy is responsible for these occurrences.

Other adverse drug reactions that have been reported in GH-treated patients include the following: 1) Metabolic: mild, transient peripheral edema; 2) Musculoskeletal: arthralgia, carpal tunnel syndrome; 3) Skin: rare increased growth of pre-existing nevi; patients should be monitored for malignant transformation; 4) Endocrine: gynecomastia; and 5) Rare pancreatitis. Of these reactions, only edema (<1% of patients) and arthralgia (4%) were reported as related to drug in the Nutropin Depot studies.

OVERDOSAGE

The recommended dosage of Nutropin Depot should not be exceeded. Acute overdosage could lead to fluid retention, headache, nausea, vomiting, and/or hyperglycemia. Long-term overdosage could result in signs and symptoms of gigantism

and/or acromegaly, consistent with the known effects of excess GH. (See recommended dosage instructions given below.)

DOSAGE AND ADMINISTRATION

The Nutropin Depot dosage and administration schedule should be individualized for each patient. Response to GH therapy in pediatric patients tends to decrease over time. However in pediatric patients, failure to increase growth rate, particularly during the first year of therapy, suggests the need for close assessment of compliance and evaluation of other causes of growth failure, such as hypothyroidism, undernutrition, and advanced bone age.

Once-Monthly Injection—It is recommended that an SC injection at a dosage of 1.5 mg/kg body weight be administered on the same day of each month. Dosages above the recommended once-monthly regimen have not been studied in clinical trials. Note: subjects over 15 kg will require more than one injection per dose.

Twice-Monthly Injections—It is recommended that an SC injection at a dosage of 0.75 mg/kg body weight be administered twice each month on the same days of each month (e.g., Days 1 and 15 of each month). Dosages above the recommended twice-monthly regimen have not been studied in clinical trials. Note: subjects over 30 kg will require more than one injection per dose.

The table below indicates the required number of injections per dose.

	Number of Injections Per Dose	
Patient Weight (kg)	0.75 mg/kg twice monthly	1.5 mg/kg once monthly
≤15	1	1
>15–30	1	2
>30–45	2	3
>45–60	2	*
>60	3	*

*Twice-monthly dosing recommended

Preparation of Dose

Nutropin Depot powder may **only** be suspended in Diluent for Nutropin Depot supplied in the kit and administered with the supplied needles.

1. Using the chart below, determine the volume of diluent needed to suspend Nutropin Depot. Withdraw the diluent into a 3 cc syringe using the needle supplied in the kit. Only the diluent supplied in the kit should be used for reconstitution, and any remaining diluent should be discarded.

Vial Size (mg somatropin)	Volume of Diluent to Be Added (mL)
13.5	0.8
18	1.0
22.5	1.2

Note: Since the suspension is viscous and prevents complete withdrawal of the entire vial contents, the vials are overfilled to ensure delivery of the labeled amount of somatropin. Using these diluent volumes for final suspension results in a final concentration of 19 mg/mL somatropin in each vial size.

2. Inject the diluent into the vial against the vial wall. Swirl the vial vigorously for up to 2 minutes to disperse the powder in the diluent. Mixing is complete when the suspension appears uniform, thick, and milky, and all the powder is fully dispersed. Do not store the vial after reconstitution or the suspension may settle.

3. Withdraw the required dose. Only one vial should be used for each injection. Replace the needle with a new needle from the kit and administer the dose immediately to avoid settling of the suspension in the syringe. Deliver the dose from the syringe at a continuous rate over not more than 5 seconds. Discard unused vial contents as the product contains no preservative. An extra needle has been provided in the kit.

Stability and Storage

Before Suspension—Nutropin Depot and diluent vials must be stored at 2–8°C/36–46°F (under refrigeration). **Avoid freezing the vials of Nutropin Depot and Diluent for Nutropin Depot**. Do not expose the Nutropin Depot vial to temperatures above 25°C (77°F). Expiration dates are stated on the labels.

After Suspension—Because Nutropin Depot contains no preservatives, all injections must be given immediately. Do not allow the suspension to settle prior to withdrawal of the dose. Suspended solution cannot be stored or used to suspend another vial of Nutropin Depot.

How Supplied

Nutropin Depot is supplied as single-use vials with 13.5 mg, 18 mg, or 22.5 mg sterile, preservative-free somatropin powder per vial.

Each 13.5 mg kit contains one single-use 13.5 mg vial of Nutropin Depot® [somatropin (rDNA origin) for injectable suspension], one 1.5 mL single-use vial of Diluent for Nutropin Depot, and three 21-gauge, 1/2" needles: NDC 50242-032-35.

Each 18 mg kit contains one single-use 18 mg vial of Nutropin Depot® [somatropin (rDNA origin) for injectable suspension], one 1.5 mL single-use vial of Diluent for Nutropin Depot, and three 21-gauge, 1/2" needles: NDC 50242-034-41.

Each 22.5 mg kit contains one single-use 22.5 mg vial of Nutropin Depot® [somatropin (rDNA origin) for injectable suspension], one 1.5 mL single-use vial of Diluent for Nutropin Depot, and three 21-gauge, 1/2" needles: NDC 50242-036-54.

Nutropin Depot® [somatropin (rDNA origin) for injectable suspension]

Nutropin Depot™ [somatropin (rDNA origin) for injectable suspension] and **Diluent for Nutropin Depot** are manufactured for:

Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080-4990

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